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RADIUM

EDITED BY
CHARLES H. VIOL, Ph. D.
AND
WILLIAM H. CAMERON, M. D.

VOL. III AUGUST, 1914 No. 5

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A MONTHLY JOURNAL DEVOTED TO THE CHEMISTRY PHYSICS AND THERAPEUTICS OF RADIUM AND RADIO-ACTIVE SUBSTANCES

RADIUM

A MONTHLY JOURNAL DEVOTED TO THE CHEMISTRY, PHYSICS AND THERAPEUTICS OF RADIUM AND RADIO-ACTIVE SUBSTANCES.

Edited and Published by Charles H. Viol, Ph. D. and William H. Cameron, M. D., with the assistance of collaborators working in the fields of Radiochemistry, Radioactivity and Radiumtherapy.

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VOL. III AUGUST, 1914 No. 5

CONTRIBUTION ON THE BIOLOGICAL AND PATHOLOGICAL ACTION OF SOLUBLE RADIUM SALTS –WITH SPECIAL REFERENCE TO ITS THERAPEUTIC VALUE IN PERNICIOUS ANAEMIA AND LEUKEMIA.

FREDERICK PROESCHER, M. D., and B. R. ALMQUEST, M. D.

The marked influence of Radioactive substances upon the circulating blood cells and the blood-forming organs is an established fact. Experimental investigation and clinical observation of *Bickel*[1], *Plesch*[2], *Falta*[3], *Gudzent*[4], and others, have demonstrated the therapeutical value of radioactive substances, especially thorium X, in the treatment of leukemia and pernicious anemia.

The effect of radioactive substances, regardless of which is used, is purely symptomatic as it exerts no direct influence upon the unknown etiological agent causing these diseases. It is no specific for any of these diseases. In spite of this, radioactive substances are the most powerful symptomatic agents used at the present time in treating pernicious anemia and leukemia.

Of all radioactive substances used, thorium X being cheaper and more readily obtained than radium salts, the majority of animal experiments and clinical observations are carried on with this agent.

For a proper comparison of the action of the thorium X in contrast to radium, we wish to refer first briefly to the biological and pathological action of the thorium x and will later dwell upon our own animal experiments with soluble radium salt and its therapeutic action in pernicious anemia and leukemia.

The Biological and Pathological Action of Thorium X

Thorium X is a decay product of radiothorium which is characterized by its short life. The exceedingly short life of thorium X permits the use of such minute quantities of thorium X that to produce 1,000,000 mache units* requires $\frac{1}{100{,}000}$ mg. thorium X against 0.6 mgm. radium bromide.

The following table illustrates the physical difference between thorium X and radium.

TABLE I.

THORIUM FAMILY OF RADIO-ELEMENTS.

	Rays	Period of Half Decay.
Thorium	Alpha	13,000 million years
Mesothorium I	.....	5.5 years
Mesotrorium II	Beta, Gamma	6.2 hours
Radiothorium	Alpha	2 years
Thorium X**	Alpha	3.6 days
Thorium-Emanation	Alpha	53 seconds
Thorium A	Alpha	0.14 seconds
Thorium B	Beta, Gamma	10.6 hours
Thorium C_1	Alpha	60 minutes
Thorium C_2	Alpha	Very short life
Thorium D	Beta, Gamma	3.1 minutes.

THE RADIUM FAMILY OF RADIO-ELEMENTS.

	Rays	Period of Half Decay
Radium	Alpha, Beta	1750 years
Emanation	Alpha	3.85 days
Radium A	Alpha	3.0 minutes
Radium B	Beta	26.7 minutes
Radium C	Alpha, Beta, Gamma	19.5 minutes
Radium D	.....	16.5 years
Radium E	Beta, Gamma	7.2 days
Radium F (Polonium)	Alpha	136 days

This table shows how much faster thorium X decays than radium. The alpha particles of thorium C^2 possess the greatest range of 8.6 centimeters. The intense energy produced by these short lived elements accounts for their intense biological action. At present we have no explanation as to how the thorium X acts upon the organism. The fatal dose for animals according to *Plesch*[5], *Karczag* and *Keetmann* shows marked individual and racial differences. They found that warm blooded animals are much more susceptible than cold blooded. The fatal dose for mice of 10 to 16 grams was 20,000 mache units. For guinea pigs weighing 50 to 200 grams 30,000 mache units. Some withstood as high as 150,000 mache units. Dogs showed same variation in dosage. A dog of seven kilograms died upon injection of 400,000 mache units. A dog of six kilograms withstood a dose of 120,000 mache units, another dog of ten and a half kilograms lived six days after the injection of 6,500,000 mache units. The autopsy of the dog showed hemorrhages in the stomach, kidneys, bladder and peritoneum. Rabbits injected with 4,000 to 20,000,000 mache units all

*Quantitative data with regard to thorium X was first given in terms of mache units (1000 X ionization current of the preparation expressed in electrostatic units), and while this is an incorrect use of the mache unit, for the sake of comparison, the data in regard to radium is given in terms of weight and also approximately in mache units.

**Thorium X used for injections contains all the remaining radio-elements of the thorium family.

lived three days, but succumbed within eight days. Spring frogs weighing from 30 to 40 grams, withstood 100,000 mache units without ill effect. The most pronounced effect of the thorium X is observed upon the leucocytes and the bone marrow. *Pappenheim* and *Plesch*[6] and also *Hirschfeld* and *Meidner*[7] found an absolute leucopenia a few days after injection of a fatal dose of thorium X. According to *Hirschfeld* and *Meidner,* all leucocytes diminished simultaneously. *Pappenheim* and *Plesch* found that the lymphocytes first disappeared followed then by the eosinophiles and monocytes and last by the polynuclear-neutrophiles. According to *Arneth*[8] rabbits, after an injection of thorium X show an absolute decrease of all leucocytes with a relative increase of the lymphocytes as well as a relative decrease in the pseudoeosinophiles. He noted also punctated erythrocytes, but no normoblast and poikilocytes.

It is of interest to note that *Arneth* observed a regeneration of leucocytes after repeated injection of thorium X. *Hirschfeld* and *Meidner* and also *Pappenheim* and *Plesch* found only a slight diminution of the red cells without any appearance of regenerative or degenerative forms. The pathological anatomical changes in animals which died following a fatal dose of thorium X, consisted in extensive hemorrhages in the lungs and peritoneum, necrotic areas in the kidneys and pancreas, and a reduction in size of the spleen and a diminution of lymphocytes in the lymph glands. The bone marrow was dark red and softened with the leucocytes almost completely destroyed.

The findings of *Salle*[9] are of interest, as he reported that after small doses of thorium X, the chromaffinity of the suprarenal-capsule was increased. In large doses he found a degeneration of cortex cells combined with hemorrhages in the cortex. He also demonstrated a decrease in the adrenalin content of the blood-serum.

According to these experiments, *Plesch*[10] estimates that the fatal dose of thorium X for an adult of sixty kilogram weight would be 10,000,000 mache units, but this dosage seems to be too high, as *Gudzent*[11] later reports a case of a woman of 47 years who died after injection of 5,000,000 mache units. The autopsy of this case was reported by *Orth*[12] and showed hemorrhages of the stomach, small intestines, colon ascendens, rectum, bladder, kidneys and liver. Therefore, we must look upon 5,000,000 mache units as dangerous to life. *Plesch, Karczag* and *Keetmann* concluded later that a dose of 1,000,000 mache units is sufficient and should not be exceeded. A period of two or three days or better two or three weeks should elapse between two injections as thorium X reaches its maximum action at the end of three weeks. The second or third dose should be two-thirds or one-half less. Thorium X, given in small doses, gives rise to no appreciable symptoms. In doses of 1,500,000 mache units, after 16 to 20 hours, a weakness accompanied by loss of appetite is observed, which is more or less annoying to the patient. This condition reaches its maximum after the second day, then disappearing and finally is followed by a temporary general improvement. The

thorium X should only be given intravenously; subcutaneous injection should be entirely avoided, as there are changes noted at the site of injection in the form of infiltration and swelling with ulceration which heals very slowly. Human beings advanced in age seem to tolerate greater doses than younger individuals. Individuals affected with tumors seem to be very sensitive to thorium X. Thorium X injections are contraindicated in enteritis, because it seemingly has a tendency to produce this condition in normal individuals, at the same time being difficult to influence by opiates. The great vulnerability of the intestinal canal to thorium X is due to its great affinity for the lymphatic structures. Almost 24 per cent of the thorium X is eliminated with the faeces. The accumulation of thorium X in the intestines should be avoided during its administration. The food stuff should be somewhat coarse so as to maintain good peristatlic action and, if necessary, a mild saline should be given. The blood picture, should be controlled daily, and if there should be a marked diminution of leucocytes thorium X administration should be stopped.

Large doses of thorium X should be given only in hopeless cases in which all other therapeutic agents have been of no avail. Thorium X is a dangerous element, it is difficult to control both on account of its accumulative effect, 88 per cent being retained in the body, and also because of its diversified action on different individuals.

Biological and Pathological Action of Radium.

In a prior communication by one of us, on the intravenous injection of soluble radium salts in human beings it was shown that the injection of one milligram of radium element in the form of radium bromide of high purity, equalling 2,700,000 mache units, caused no deleterious effects. For the approximate establishment of the maximum dose of radium element in human beings, a number of animal experiments were conducted on white mice and white rats for estimating the fatal dose, the action on the blood and the pathological changes in the organs. Radium was used in the form of a soluble radium bromide and injected subcutaneously. The following table shows the quantity of radium used, in white mice and rats, and the time which elapsed between the injection and death.

TABLE II.

ESTIMATION OF FATAL DOSE OF RADIUM ELEMENT FOR WHITE MICE.

Mouse	Weight Grams	Amount of Radium Element Given Subcutaneously in Form of Radium B'mide	Date of Injection	Died	Lived Days	Weight at Death Grams	Amount of of Radium Pro 1,000 gr. Living Wt.
		1 Microgram				45.5	Micrograms
No. 1	22	2,700 M.U.	2- 3-14	6-22-14	139		123,000 M.U.
		3 Micrograms				136.30	Micrograms
No. 2	22	8,100 M.U.	2- 3-14	4-27-14	83		368,000 M.U.
		5 Micrograms				227.5	Micrograms
No. 3	22	13,500 M.U.	2- 3-14	5-24-14	141	10	615,000 M.U.
		10 Micrograms				455	Micrograms
No. 4	22	27,000 M.U.	2- 3-14	4- 6-14	62		1,230,000 M.U.
		20 Micrograms				2,000	Micrograms
No. 5	20	54,000 M.U.	3-24-14	4-23-14	31	16	2,700,000 M.U.
		25 Micrograms				1,250	Micrograms
No. 6	20	67,500 M.U.	3-24-14	4-12-14	19		3,375,000 M.U.

		30 Micrograms					1,500 Micrograms
No. 7	20	81,000 M.U.	3-24-14	4-17-14	24		4,050,000 M.U.
		50 Micrograms					2,083 Micrograms
No. 8	24	135,000 M.U.	4- 8-14	4-18-14	10		5,624,100 M.U.
		50 Micrograms					2,083 Micrograms
No. 9	24	135,000 M.U.	4- 8-14	4-17-14	9		5,624,100 M.U.
		100 Micrograms					3,846 Micrograms
No. 10	26	270,000 M.U.	4-30-14	5- 7-14	7	18	10,390,000 M.U.

TABLE III.

ESTIMATION OF FATAL DOSE OF RADIUM ELEMENT FOR WHITE RATS.

Rat	Weight Grams	Amount of Radium Element Given Subcutaneously in Form of Radium B'mide	Date of Injection	Died	Lived Days	Weight at Death Grams	Amount of of Radium Pro 1,000 gr. Living Wt.
		40 Micrograms					328 Micrograms
No. 1	122	108,000 M.U.	3-25-14	5-16-14	52	102	886,000 M.U.
		60 Micrograms					490 Micrograms
No. 2	122	162,000 M.U.	3-25-14	5-15-14	51	90	1,330,000 M.U.
		80 Micrograms					640 Micrograms
No. 3	125	216,000 M.U.	3-25-14	5- 9-14	45	90	1,730,000 M.U.
		100 Micrograms					820 Micrograms
No. 4	122	270,000 M. U.	3-25-14	4-20-14	26	66	2,215,000 M.U.
		150 Micrograms					909 Micrograms
No. 5	165	405,000 M.U.	4- 4-14	5-19-14	45	136	2,455,000 M.U.
		200 Micrograms					1,333 Micrograms
No. 6	150	549,000 M.U.	4- 4-14	5- 5-14	31	104	3,000,000 M.U.

As shown by Table II, an exact determination of the fatal dosage of radium salts for white mice, is a difficult matter. In small quantities from 1-5 micrograms, there seems to be no regularity between the time of death and the amount of radium injected. Mouse No. 1, which received 1 microgram, died after 146 days, while Mouse No. 2, which received 3 micrograms, died after 86 days, and Mouse No. 3, which received 5 micrograms, lived 141 days; almost as long as Mouse No. 1 receiving only 1-5 of the dosage. With 10-50 micrograms there seems to be a certain relationship between the time of death and amount of radium injected, as the mouse which received 10 micrograms lived about 6 times as long as Mouse No. 8 with 50 micrograms. Mouse No. 10 with 100 micrograms, lived 7 days; almost as long as Mouse No. 9 and 10 with an average lifetime of 9.5 days. In the case of white mice beginning with 50 micrograms, there appears to be a certain constant life period which is not appreciably affected by increased doses of radium. Mice Nos. 8 and 9 lived on an average of 9.5 days. Mouse No. 10, with a double dosage of radium, lived 7 days, showing no great difference in the life period, while with smaller doses the duration of life in days appears to be a function of the amount of radium injected. The same law seems to be true for other animal species, for instance, white rats. As shown in Table No. III there seems to be no appreciable difference between the limits of 40 to 200 micrograms, in the time of death after the injection of different amounts of radium; if we take in consideration the individual and race differences, *Plesch, Karczag* and *Keetman* made analogous observation with rabbits, which were injected with thorium X in quantities from 50,000-20,000,000 mache units. All animals lived for a period of three days, but died within eight days. All animals showed a marked reduction of their body weight at time of death. It is regretable that *Plesch, Karczag* and *Keetmann* have not given more exact data, as to how long their animals

lived after injection of thorium X; a comparison with our experiments is therefore not possible.

Before considering the question what is the fatal dose of radium element for human beings, we wish to report first the animal experiments, with special reference to the changes upon the circulating bloodcells, and the pathological findings in the organs. The following tables illustrate the effect of large doses of radium upon the circulating bloodcells of white mice and rats. In the mouse experiments we studied the effect of the radium on the bloodcells only in Mice Nos. 8, 9 and 10, which received 50 and 100 micrograms of radium element. In the rat series we made a complete examination of the blood of all the animals at intervals until death occurred. The blood was taken from the tail. The haemoglobin was estimated with the Fleischel-Miescher haemoglobinometer, the counts of the white and red cells were made with the Buerker counting chamber, the smears were stained with a methyl alcohol solution of eosin-methylen-toluidin-blue and Giemsa solution.

In the following table is given the data obtained in the experiments on the mice and rats:

TABLE IV.

RADIUM MOUSE No. 8.

Date	Haemoglobin	Red Cells	White Cells	Neutrophiles	Eosinophiles	Lymphocytes	Small	Medium.
4- 8-14	18.24 gm.	7,000,000	19,000	21.00	7.55		46.00	25.55
	50 micrograms radium (element) subcutaneously.							
4- 9-14			6,562	59.00	5.00		8.00	28.00
4-10-14	12.84 gm.	11,850,000	3,500	29.37	0.62		53.14	16.87
4-11-14	12.56 gm.		1,750	40.00			45.00	15.00
4-13-14	12.84 gm.		875	13.46			86.54	
4-14-14	10.76 gm.	10,315,460	250	2.28			88.63	9.09
4-15-14			250	10.00			88.00	2.00
4-16-14			200			Lymphocytes Only		
4-17-14	6.56 gm.	5,400,000	100			Lymphocytes Only		
4-18-14	5.40 gm.	3,672,000	200			Lymphocytes Only		

RADIUM MOUSE No. 9.

Date	Haemoglobin	Red Cells	White Cells	Neutrophiles	Eosinophiles	Lymphocytes	Small	Medium.
4- 8-14	17.96 gm.	13,025,000	25,012	17.50	7.25		38.50	36.75
	50 micrograms radium (element) subcutaneously.							
4- 9-14			5.625	17.50	6.00		18.00	58.50
4-10-14	12.84 gm.	8.175,000	3,375	49.00	0.50		29.50	21.00
4-11-14	11.04 gm.		3,750	61.00			37.00	2.00
4-13-14	12.84 gm.		500	6.67			80.00	13.33
4-14-14	12.56 gm.	8,087,500	187	6.00			85.00	9.00
4-15-14			273			Lymphocytes Only		
4-16-14			125			Lymphocytes Only		

RADIUM MOUSE No. 10.

Date.	Haemoglobin	Red Cells	White Cells	Neutrophiles	Monocytes	Lymphocytes	Small	Medium.
4-30-14	14.64 gm.	10,800,000	11,625	38.00	0.50		59.00	2.50
	100 micrograms radium (element) injected subcutaneously.							
5- 1-14	13.76 gm.	10,800,000	4,000	24.00	2.00		69.00	5.00
5- 4-14	13.76 gm.	10,875,000	1,125	15.00			83.00	2.00

RADIUM RAT No. 1.

Date	Haemoglobin	Red Cells	White Cells	Neutrophiles	Eosinophiles	Lymphocytes	Large	Small	Medium	Basophiles
3-25-14	16.44 gm.	8,784,000	23,000	21.00	5.00	1.33	46.68		25.00	0.33
	40 micrograms radium (element) subcutaneously.									

4- 1-14	16.76 gm.	9,640,000	4,400	20.00			74.37	5.33	0.30
4- 6-14			4,125	7.50	1.00	1.50	30.00	60.00	
4- 8-14			5,625	24.81	2.00		14.66	58.00	
4-10-14	14.04 gm.		3,500	12.50	0.50		33.00	54.00	
5 -4-14	13.46 gm.	8,500,000	9,750	32.50	4.50		48.00	15.00	

RADIUM RAT No. 2.

60 micrograms radium element.

Date	Haemo-globin	Red Cells	White Cells	Neutro-philes	Eosino-philes	Lym-phocytes	Large	Small	Medi-um	Baso-philes
3-25-14	12.56 gm.	7,744,000	26,533	16.80	0.12			56.80	26.22	
	60 micrograms radium (element) subcutaneously.									
4- 1-14	11.96 gm.	8,326,000	7,533	15.66	1.33				38.00	0.33
4- 6-14			6,203	26.66	0.66	1.00		46.35	28.00	
4- 8-14			6,687	15.00	0.50	0.25		59.50	24.75	
4-10-14	9.56 gm.		7,500	15.00				43.00	42.00	
4-21-14				30.50	2.00			51.50	16.00	

RADIUM RAT No. 3.

Date	Haemo-globin	Red Cells	White Cells	Neutro-philes	Eosino-philes	Lym-phocytes	Large	Small	Medi-um	Baso-philes
3-25-14	14.36 gm.	8,560,000	22,533	17.77	2.77			62.45	16.50	0.50
	80 micrograms radium (element) subcutaneously.									
4- 1-14	14.04 gm.	8,724,000	3,983	11.00			0.50	65.50	22.00	
4- 6-14			4,250	7.00	1.50		0.50	33.75	53.50	
4- 8-14			3,560	6.00	1.50		0.50	50.50	41.50	
4-10-14	10.16 gm.		2,000	12.00	2.00		0.50	49.50	36.00	
4-20-14	11.36 gm.	6,457,000	5,375	39.00	0.33			38.36	22.31	
5- 9-14	6.28 gm.	3,225,000	7,250							

RADIUM RAT No. 4.

Date	Haemo-globin	Red Cells	White Cells	Neutro-philes	Eosino-philes	Lym-phocytes	Large	Small	Medi-um	Baso-philes
3-25-14	15.24 gm.	7,632,000	25,600	23.37	0.33			49.00	26.31	0.33
	100 micrograms radium (element) subcutaneously.									
4- 1-14	14.96 gm.	8,056,000	6,133	19.31	0.33		4.00	32.42	43.80	
4- 6-14				10.00	1.00			49.00	40.00	
4- 8-14	7.76 gm.		3,125	5.50	0.50		1.00	61.00	32.00	
4-10-14	8.64 gm.		4,203	64.28	0.95			64.28	23.33	
4-20-14	8.90 gm.	5,550,000	16,312	24.00				52.00	24.00	

RADIUM RAT No. 5.

Date	Haemo-globin	Red Cells	White Cells	Neutro-philes	Eosino-philes	Lym-phocytes	Large	Small	Medi-um
4- 4-14	17.04 gm.	7,500,000	23,687	21.33	2.33		.66	54.33	21.33
	150 micrograms radium (element) subcutaneously								
4- 5-14			14,000	48.37	11.00		0.66	24.66	15.31
4- 6-14			12,062	41.00	9.66			9.33	40.01
4- 7-14			7,562	10.68	6.33			70.66	12.33
4- 8-14			5,873	3.50	3.00		.05	67.45	26.00
4-10-14	11.04 gm.	9,150,000	3,250	3.16	0.53			87.89	8.42
4-11-14	16.16 gm.		3,054	5.00	1.00			80.50	13.50
4-13-14	10.16 gm.		3,125	9.50	1.50			69.50	19.50
4-21-14	12.26 gm.	7,137,500	4,656	4.00	1.00			81.00	14.00
4-29-14	14.36 gm.	8,100,000	4,687	14.50	3.50			71.00	12.00

RADIUM RAT No. 6.

Date	Haemo-globin	Red Cells	White Cells	Neutro-philes	Eosino-philes	Lym-phocytes	Large	Small	Medi-um
4- 3-14	19.72 gm.	11,050,000	23,500	16.00	2.20		2.10	50.30	29.40
4- 4-14	19.44 gm.	11,264,000	29,750	14.60	4.00		.02	49.85	30.40
	200 micrograms radium (element) subcutaneously.								
4- 5-14			16,000	51.68	2.33		1.00	26.66	18.33
4- 6-14			9,437	46.50	1.50			34.50	18.00
4- 7-14			4,625	37.99	0.59		0.59	36.74	24.09
4- 8-14			3,437	7.00	3.50			55.00	34.50
4-10-14	11.36 gm.	9,400,000	2,687	3.00				73.50	23.00
4-11-14	12.56 gm.		2,125	17.36	0.53			72.64	9.47
4-13-14	9.56 gm.		1,687	18.01			10.45	45.06	36.48
4-21-14	13.76 gm.	6,612,500	6,562	50.00				38.00	12.00
4-29-14	11.96 gm.	6,962,500	6,750	48.00	2.50			31.00	18.00

(To be continued in next number.)

Radium Production in America

Charles H. Viol, Ph. D.

The illustration shown is reproduced from a photograph* of

a dish of radium bromide. This material represents the radium output of the Radium Research Laboratory of the Standard Chemical Company from June 10th to July 1st, 1914. The small silica capsule which is shown in its natural size, contains 1764 milligrams of anhydrous radium barium bromide having a radium element content of 740 milligrams. (International gamma ray Standard). Since pure anhydrous bromide contains 58.6 per cent of radium element, the 740 milligrams of radium correspond to 1263 milligrams of pure anhydrous radium bromide and the salt shown is 71.6 per cent pure radium bromide. The radium shown in the dish represents months of work on upwards of three hundred tons of Colorado carnotite ore. In the process of extracting this radium over five hundred tons of chemicals were used, exclusive of water. When one considers the enormous difficulties and expense in extracting this small quantity of radium salt from such huge amounts of material, it is possible to realize why radium salts are so costly. At the rate of $120 per milligram of radium element, which is equivalent to a rate of $64.35 per milligram of pure crystalline radium bromide, ($Ra\ Br_2\ 2H_2O$, the pure "radium" of commerce in the past), the radium shown in the dish has a value of $88,800. The total radium output of the Standard Chemical Company for June, 1914, in the form of radium prep-

*The photograph of the radium salt was made shortly after the salt had been crystallized and dried. Under these conditions the beta and gamma ray activity of the radium was at a minimum and therefore the photographic plate could be brought near the preparation without risk of fogging.

arations of a high purity, (60 per cent or purer) amounted to 1114 milligrams of radium element which is equivalent to 2077 milligrams of pure crystalline radium bromide, Ra Br_2 $2H_2O$. Up to May 1st, 1914 (cf. Eng. & Mining Journal, July 4th, 1914, pp. 25-6) the total production of radium in the form of salts of high purity amounted to 4563 milligrams of radium element, equivalent to 8,530 milligrams of pure crystalline radium bromide. From May 1st, to July 1st, 1914, there has been produced 2046 milligrams of radium element equivalent to 3817 milligrams of pure crystalline radium bromide. This makes the total production to July 1st, 6609 milligrams of radium element of which 5229 milligrams of radium element were contained in the product obtained between January 1st and July 1st, 1914.

The Austrian Government—the largest European producer of radium—obtained 2014 milligrams of radium element in the salts produced in 1911 and 1698 milligrams of radium element in 1913. The data on production in 1913 is not yet available so far as the writer is aware, and while strenuous efforts were being made to increase the output in 1913 and 1914, it is doubtful whether more radium will be obtained than in preceding years. The Austrian radium is produced from the Joachimsthal pitchblende. Other European producers use Cornish pitchblende, and Portuguese autunite. Considerable Colorado carnontite was shipped abroad in 1912 and 1913. At present, however, the greater part of the Colorado ore is being treated in the United States and as shown by the above figures the radium output of the Standard Chemical Company is many times greater than the output of all the European producers.

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Reviews and Abstracts

W. H. B. *Aikins.* The Value of Radium in Malignant Gynaecological Conditions. The Canadian Lancet. Vol. 47, pp. 742-48 (1914). A brief resume of the work of *Abbe, Wickham and Degrais, Rubens, Duval* and *Cheron, deCourmelles, Schauta, Latzko, Doederlein, Wertheim, Bumm, Kroenig* and *Gauss, Werner* and others, where radium has been used in the treatment of cancer of the uterus. Summing up the work *Aikins* says, "practically all writers on the subject are agreed that as regards gynecology radium has its chief field of usefulness in inoperable cases and as a prophylactic against recurrence after radical operation, and that in such cases its value as an adjunct to treatment is inestimable. The growth should be completely or partially removed in all cases in which such a procedure is possible, and radium treatment in such cases should replace operation only when the particular circumstances in a given case under the risks of operation are greater than those which would be incurred by the possibility of an operable case becoming inoperable whilst radium treatment was being tried." "The advantages of radium as com-

pared with the X-ray are that radium possesses greater power of penetration, the facility with which it is applied, and the fact that in radium we are dealing with a substance the dosage of which can be easily controlled." A bibliography of twenty-two articles cited, is given.

* * * * *

Radium Therapeutics. By N. S. *Finzi,* M. B. (Lond.), M. R. C. S., L. R. C. P., L. S. A., Chief Assistant in the X-ray Department St. Bartholomew's Hospital. Oxford University Press, Publishers, American Branch, 35 West Thirty-second Street, New York City. 1913. Price, cloth $2.00. A book of over a hundred pages in which is briefly given a clear account of the uses and action of radium and its rays. The book is divided into six chapters which are as follows: Introduction; Internal administration of Radium; Histological, Physiological and Pathological action of Radium Radiations; Apparatus and Methods of Application; Treatment of Superficial Diseases; Treatment of Internal Diseases; Appendix—Other Radioactive Substances. This work is well worth a physician's reading, if he wishes to learn something of the radioactive substances, their rays and the therapeutic effects of these rays.

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P. *Degrais* and A. *Bellot.* Cancer of the Uterus and Radium: Clinical and Histological Considerations. (Edited and arranged by W. H. B. *Aikins*). Canadian Practitioner and Review. Vol. 39, pp. 334-48, (1914). The authors discuss the treatment of inoperable epithelioma of the cervix, sarcoma of the uterus and postoperative recurrences by the local application of radium. The histological changes caused by the action of the radium rays on malignant cells is discussed and then are given some general conclusions, where we learn that "Upon the results obtained in operable cancer of the cervix and in recurrences, and upon the indubitable proofs of the action of radium upon the cancer cell, *it appears to us legitimate to base the adoption, as a routine procedure, of vaginal irradiation after every ablation of the cancerous uterus.* It also seems to us that in surgical technique, as for instance after the removal of the breast, we should not deprive ourselves of the resources of radium, which is capable of transforming beneficially an area in which some cellular remnants might induce an unfortunate recurrence of the neoplasm."

"Radium is likely to play its role so much the better, the more the neoplasm has been reduced to an appreciable minimum by a surgical operation. We say that *the latter may be facilitated or even rendered possible by radium, which, in certain cases, modifies an inoperable neoplasm to such an extent that it becomes operable.* Such cases, above all others, would be amenable to post-operative irradiation."

"In spite of our long period of personal practice we have been unable to formulate any statistics, owing to the fact that the cases differ so much from one another, and we can here give only a general summary of facts reflecting the general impression which has

been made upon us by the numerous cases of cancer of the uterus or of recurrence which we have treated with radium."

"Excluding cases in which the lesions have deeply invaded the true pelvis and the gaglia, and those in which extensions to the bladder and rectum render any attempt to complete treatment of the neoplasm impossible, it may be said that the distressing symptoms and haemorrhage have invariably been greatly relieved by the application of radium."

"Although we emphasize the value of radium therapy, we do not for a moment intend to claim that radium plays the role in the cure of cancer. Our present object is to render obvious its value as a new therapeutic agent, which is capable of rendering services to the patient, such as can be rendered by no other method of treatment, excepting always those which can be rendered by surgery in operable cases."

"Without wishing to revert here to the special practical facilities of the armamentarium of radium therapy, we think it desirable, whilst doing justice to the painlessness of the applications, to point out a few manifestations inherent in the treatment, which it is essential to recognize and take into consideration. Even during the applications the patients may experience a sensation of nausea, which in certain cases results in vomiting, but which otherwise disappears very rapidly."

"During the following days the patients may complain of very marked prostration. It is advisable to warn them of this, in order that this symptom, which is moreover quite transitory in duration, should not discourage them in regard to the future. Finally, in ten to fifteen days after the applications there are symptoms of remote reaction, showing themselves on the part of the bladder and rectum by a frequent desire to micturate and defaecate, as well as by the emission of muco-membranes. These symptoms remain acute for eight to ten days, after which they disappear, leaving no trace."

"In conclusion it may be said that although extraordinary retrogression and considerable prolongation of life have been observed, sometimes even in desperate and fatal cases, it is particularly essential, in dealing with this subject, to carefully weigh the reservations which *Wickham* and ourselves have always made in regard to cancer, and to consider the satisfactory results in cold blood."

"We may add that the interest of radium treatment of cancer of the uterus, apart from the method of application, is dependent also in a marked degree on the utilization of the method of surgery-radium-therapeutics. The role of radium is to frequently come to the assistance of surgery, immediately after curettage, partial extirpation of the uterus or total hysterectomy; or before operation with the object of rendering operable a tumor which is inoperable or can only be operated upon with difficulty."

"In every way radium may intervene to relieve the patients and to prolong their existence under more tolerable conditions. This applies even to desperate cases, associated with repeated haemorrhages or intolerable pain."

W. S. *Lazarus-Barlow.* The Cause and Cure of Cancer Viewed in the Light of Recent Radio-Biologic Research. British Med. Journ. May 9th, pp. 1001-6 (1914). The author made this the subject of an extended address before the Leeds Medical Society, and while speaking mainly from the standpoint of biological research, developed much of a highly interesting character in the way of reflections.

In the theme of radiations as a causative agency in cancer, he is dealing with an old favorite of his and feels that the developments of the past five years link radioactivity and cancer more closely than ever. From certain facts and suggestions he builds his theory, more interesting from the point of view of hypothesis than of demonstration to be sure, but nevertheless well defended.

Noting the great diversity of tumor growth which, roughly, may be separated into three sub-groups, carcinoma, sarcoma and non-malignant, he emphasizes the fact that the primary stimulation to those diversified systems of growth looks for its origin to the union of a single spermatozoon with a single ovum. Thus the great variety in growths must be traceable to some added stimulation which is purely local in its origin; it is possible that a fundamental fact or a few fundamental facts underlie the whole complexity.

Thus radiations and more particularly radium radiation might be the agency to serve as a cause of cancer, to the exclusion of all others.

Correlated facts to support this assumption are as follows:—

1. That radium is widely distributed throughout nature in quantities which have been shown capable of accelerating division of cells. 1/100 millionth of a milligram of radium is detectable while 1/500 millionth milligram can be quantivated.

Even such small amounts as these (as in rocks) can cause cell division in the ova of the ascaris.

Collateral evidence along the same lines is contributed by the practical use of radium; where stimulation of both cancerous and connective tissue cells is observed after radiation. In the vegetable kingdom the stimulation of growth likewise furnishes inferential evidence. The author himself has demonstrated that radium causes a stimulation of muscular tissues, so that it lives longer.

There is to be sure, a wide variation in the amount of radium needed for cell stimulation (and this he holds points to selective action on the part of radium) but there is plenty of evidence that a wide variety of cell stimulation is possible if an accurately adjusted amount of radium is used.

2. Bacteria suspended in a radium-containing fluid collect radium from that fluid and can be shown to contain a greater percent of radium than the fluid itself. The bearing of this fact on the question lies in the well recognized influence of traumatism and inflammation in the development of cancer. Such processes would imply the growth of bacteria, the presence of which would in turn increase the radioactivity of the nidus.

3. Alpha rays cause disappearance of *Altmann's* granules from normal cells thus rendering them, in respect to this element, identical with malignant cells, which do not show the granules.

4. While radium is detectable in normal tissue it is present in much smaller quantities than in cancer tissue or in the tissues of carcinoma patients. Gallstones associated with carcinoma of gall bladder show relatively large amounts of radium, while simple stones show little or none. Since a stone does not disintegrate, this amount of radium may be assumed to be original content, while in broken down and otherwise cancerous tissues there is the opportunity for escape of radium content.

5. The analogy to X-ray on the production of cancer in workers; since the cases have been from four to fourteen years in developing the author expects that, given time, cancer in workers will be laid at the door of radium.

6. Nor are these minute quantities of radium negligible. Small as they are they are capable of great traumatism. Thus the 1/100 millionth milligram in a gall stone will throw out 100,000 combined rays in twenty-four hours at a velocity of 12,000—180,000 miles per second and this without taking account of secondary radiation.

Thus in vulnerable tissues a race of cells may be stimulated to arise, in which rapidity of division dominates.

As to the treatment and cure of cancer with radiation, the author still speaking from the biological viewpoint, shows how practice must in all cases link itself with what the laboratory may be able to point out as to indications and advantages.

1. A sufficient dose of radium and other radiation is capable of killing every type of cell met with in cancer. But in this connection it must be borne in mind that different rays have different capacities according to the different content of energy and extent of their range. To illustrate, stimulation of the ascaris ovum requires 100 times as much radioactive element, if the alpha rays are excluded.

2. Action of radiation on cells is selective i. e., all varieties of cells are not equally affected.

a. A clinical illustration of this would be the action of the X-ray in ringworm of the scalp where the cells of the hair follicles are killed, and the hair drops out, but nothing else is affected.

b. Another point is the affinity of radiation for the testicles and ovaries with sterility as a sequence.

c. The influencing of the spleen by radiation as in leukemia (the author suggests that it may be due to secondary rays produced by the iron present).

d. Laboratory confirmation. *Hertwig* can produce at will, by regulation of dosage, his so-called "tadpole disease." The vulnerability of rat sarcoma to radiation is twenty-four times that of leucocytes. The demonstration that along with the death of cancer cells there is a stimulation of connective tissue cells and of white corpuscles.

Selective action must be of fundamental importance. Practically we may make a broad grouping, viz:

Rodent cancer and round celled sarcoma is highly susceptible to attack.

Squamous epithelioma fairly susceptible.

Spheroidal carcinoma somewhat susceptible.

Columnar carcinoma little susceptible.

Practically, the inserting of a tube into a growth so as to get uniform radiation is but to repeat the laboratory experiences, and in results will as surely demonstrate selectivity.

3. There is some evidence of the production of an immunity along the lines of antibodies and autogenous vaccines.

a. Because as an agent of mere destruction i. e., in doses sufficient to produce necrosis, radium is not better than any other agents.

b. If we can prove it selective that would mark some superiority to other agents destructive in their scope.

c. But to demonstrate the production of immunity we must show the creation of an antibody and this the author declares the whole crux of the question of the value of radiation. In his opinion the evidence though small is quite cogent.

1. Mouse cancer cells exposed to a substantial amount of radiation are inoculated on one side of a mouse: a graft of mouse cancer on the opposite side of the animal will not take. The degree of immunity follows a curve that corresponds to the gradation of the dose. The cancer cells must be living. (In this connection compare *Wasserman's* experiment where he showed the possibility of taking the malignancy out of mouse cancer cells without destroying their viability. Abstract in May, 1914, "Radium." Ed.).

2. In practical work, radiation of a neoplasm has caused adjacent, even distant, glands to disappear—since 80 per cent of glands are neoplastic and the distance was beyond the reach of the rays, the inference is justified that there is at work some agency operating through the blood.

3. The general testimony of the laboratory investigators of vaccines and antibodies is that cancer will produce an antibody under the influence of modified metabolism. This antibody is likely to be highly specific, as in autogenous vaccines. The differing strains of mouse cancer reproduce only themselves. Thus histological similarity does not imply biological identity. Hence it is likely that A's cancerous cells will be influenced only by an antibody produced in A. It is not then probable that we can secure passive immunity to cancer or that an anticancerous serum can be developed. The practical conclusion of this reasoning is that to each variety of cancer we must adapt a method; even further, it may be said, to each case.

To produce destruction of some cells:—

1. We must procure only a diminished vitality in others, to the end that an antibody may develop.

2. We must do a minimum amount of damage to non-cancerous tissue.

In the search for this adaption we must be prepared for:—

—Sloughing within the tumor.
—Sloughing of non-malignant tissues.
—Septic absorption.
—Failure to react to radiation.
—Intense fibrosis.
—Temporary improvement with recurrence later.
—Haemorrhage, etc.

These disasters are however, but necessary concomitants of pioneer work and may well become things of the past. In conclusion there follow practical hints of great value.

1. Every case should be subjected to an histological control. The examination for *Altmann's* granules is fundamental for the differentiating between sarcoma and inflammatory tissue. Two cases of reported cure showed unmistakably in the microphotographs that the underlying process was inflammatory.

2. The amount of radium should be periodically verified. The author cites a long paper, pessimistic in its conclusions because of failure, in which case the reputed two packages of radium, of 250 and 150 milligrams respectively, turned out to be 2½ and no milligrams respectively. It is also to be remembered that radium may be lost through a crack or break in the solder.

3. Important to recognize that metabolic processes are profoundly disturbed after radiation. That with reduction of the size of the tumor a great and sudden influx of septic material may discharge into the economy; that there are also considerable changes in the blood after radiation. Thus we may meet death from sepsis, or a temporary well-being which may represent a limited autointoxication.

4. Surgical operations after radiation should not be carried out until sufficient time has elapsed for a restoration of general health. In this connection he recalls several cases of inoperable tumors rendered operable, where, the operation being at once entered upon, death ensued, but not on surgical grounds. The longer the temptation to operate is resisted the better the prospect.

5. Repeated doses of irradication should be given only with great care and with sufficient interval.

6. Conversely, radiation should not immediately follow operation. The two last propositions connect themselves closely with the author's conception of an antibody.

This cannot be developed by dead cells and would thus connect closely with the diameter of the mass of malignant cells radiated.

Ideally, the peripheral cells should be so affected as to produce an antibody which would oppose the malignant cells that threaten to extend out. (This would suggest in practice the removal or necrotizing of the bulk of the growth, with radiation of the outer shell. Ed.).

The radiator must steer then between the Scylla of Extensive Destruction of both normal and malignant tissue, with the result of no antibody, and the Charybdis of Insufficient Modification of cells, with just enough injury to make of them only latent cancer cells, and the end result of stimulating growth.

(All this points to the importance of method and the overwhelming factor of the personal equation and individual experience. Thus radiation is not for every practitioner. Ed.). Samuel *Delano.*

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Theodore W. *Richards* and M. R. *Lembert.* The Atomic Weight of Lead of Radioactive Origin. Journ. Am. Chem. Soc., Vol. 34, pp. 1329-1344. (1914).

"It has been pointed out by many of the workers upon radioactivity, especially by *Boltwood, Ramsay, Rutherford* and *Fajans,* that the most conclusive test concerning the recent theory of the degeneration of radio-active elements is to be found in the determination of the atomic weights. If each alpha-transformation involves the loss of an atom of helium and nothing else which is weighable, the atomic weight of the product should be just 3.99 less than that of the original substance, because 3.99 is the atomic weight of helium developed during the alpha-transformation. Thus, if radium has an atomic weight of 225.97, its emanation ("niton") should have an atomic weight of 221.98, radium D (which is supposed to involve three more alpha-transformations) should be 210.01; and radium G (yet another alpha-transformation) should be 206.02.

"Still more recently, a further theory, which has been independently proposed by *Fajans,* and by *Soddy,* indicates that some of the places in the periodic table, corresponding to high atomic weights, should perhaps each include several elements, different in atomic weight but very similar in other properties. Thus, in the place which we usually asign to lead, we should expect to find a mixture of ordinary lead, radium B, D, and G, and perhaps, also at least one other radioactive product from thorium and one from actinium. These different substances, according to the hypothesis, should have identical spectra and be inseparable by chemical means, but, coming from different sources, they should have different atomic weights. The theory supposes that each alpha-transformation involves a loss of valence of two, and each beta-transformation a gain of valence of one. The beta-transformation involves no change of weight. Thus radium D (supposed to have an atomic weight of 210) after two beta- and one alpha-transformations returns again as radium G to the same place in the periodic system with an atomic weight of only 206. This place is

that assigned to lead (which some suppose to be primarily radium G), the only one of the radium series possessed of a long life and not highly radioactive.

"The problem is one capable of a decisive gravimetric test; specimens of lead, consisting of different mixtures, obtained from different sources, should have different atomic weights."

The atomic weight of a number of samples of lead of radio-active origin was determined with the following results:

Source of Lead.	Atomic Weight.
Lead from North Carolina uranite	206.40
Lead from Joachimsthal pitchblende	206.57
Lead from Colorado carnotite	206.59
Lead from Ceylonese thorianite	206.82
Lead from English pitchblende	206.86
Common lead	207.15

"It was found that all of the radioactive specimens possess a lower atomic weight than ordinary lead, as determined under identical conditions, the deficiency in one case amounting to as much as 0.75 of a unit."

"No simple linear quantitative relationship between the exact amount of radioactivity and the atomic weight was found. The radioactivity of the various samples was compared by means of the quantitative electroscope."

"This amazing outcome is contrary to Harvard experience with several other elements, notably copper, silver, iron, sodium, and chlorine, each of which seems to give a constant atomic weight, no matter what the geographical source may have been."

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Samuel *Stern*. The Present Status of the Non-Operative Treatment of Bengin and Malignant Growths, as seen at the Clinics Abroad. Medical Record. Vol. 85, pp. 615-19 (1914). The writer has the following to say with regard to the use of radium and mesothorium in the treatment of malignant growths:—

"Ever since the Congress at Halle, when men of world-wide reputation announced that in radioactive substances at last we have found an agent which was designated to relegate the surgeon to oblivion in the treatment of these cases, it has become the most widely discussed question in medical science. The tremendous enthusiasm which arose at the time was rather unfortunate, as the world accepted the announcement literally and expectations arose to such a high pitch that reaction was bound to follow."

"When I reached Europe in September, I found that the reaction was already setting in, and the extreme wave of enthusiasm displayed at the time of the Congress had decidedly cooled off. They began to realize the limitations of the treatment, and also the fact that the subject was in the experimental stage, and that only years of experimenting could prove its real value. Fortunately this wave of reaction did not have the effect of discouraging further work in this field, but quite the reverse, it acted as a stimulant toward developing mature and serious investigation in every direction."

"I found that practically all hospitals and clinics were either already equipped to do work with radio-active substances or were

straining every effort towards doing so. In fact the universal cry one hears everywhere is for more mesothorium and more radium."

"Almost every clinic has its own individual technique of administration. I found the greatest divergence of opinion as to the following: (1) Dosage—This varies between 3,000 and 20,000 mgm. hours. (2) Filters—The filters generally in use are lead, silver, gold, platinum, and bronze. (3) Method of protecting the surrounding areas."

"They all seem to agree on the following points: (1) Radioactive substances should be used as highly concentrated as possible. (2) They should not cover a large surface but should be kept in as small a container as will hold them. (The higher the concentration the deeper the penetration.) (3) Less than a certain amount (50 to 100 mgm.) should never be used in the treatment of internal carcinoma. (4) Practically no difference can be seen between the action of mesothorium and that of radium."

"*Bumm* in Berlin has 650 mgm. of mesothorium divided into 50 mgm. capsules. At first he used from 300 to 450 mgm. doses, but found that the bladder and rectal tenesmus produced by the application was so serious that he had to diminish his dosage. At present he uses 100 to 150 mgm. doses for 10 hours, repeating every second day until they had from 10,000 to 20,000 mgm. hours."

"The mesothorium is in 1 mm. silver capsules covered with rubber. This is inserted into the cervix, which is covered entirely with a 3 mm. cup-shaped lead stopper, also covered with thick rubber—the rest of the vagina is well packed with gauze to keep this in place. He gets his dermatitis after three or four applications but disregards this entirely and persists with the treatment. Even with the small doses he still gets considerable tenesmus but disregards this also, except when it is very severe."

"In connection with this the patients get daily X-ray treatments with a high-vacuum tube to different fields and per vaginam through a lead-glass speculum. After a full dose is given treatments are discontinued for about two weeks and then repeated."

"*Bumm* had treated about eighty cases up to the time of my visit. While his immediate results were fairly good, I found that he had lost a great deal of his enthusiasm. Recurrences were beginning to appear, especially in the younger patients. In two cases he had perforations into the intestines, and in two or three other cases bad rectal strictures occurred. The amount of tenesmus produced is still very severe."

"I think many of these mishaps were due to the secondary rays from the heavy lead stopper he used. At any rate in the other clinics I visited where lead stoppers were not used, I found decidedly fewer complaints of tensemus and other accompanying symptoms."

"When I visited *Latzko*, he was just ordering some 3 mm. nickel-plated bronze filters. This is on the principle that secondary rays are produced in metals in direct ratio to their atomic weight, and when two metals are amalgamated the secondary rays produced by the heavier metal are absorbed by the lighter

one. He never uses more than 3000 mgm. hours followed by 2 or 3 week pause. He thinks that larger doses should be very rarely used."

"*Doederlein* still retains some of his enthusiasm, although he is not quite as positive in his statements now as he was at the Congress. No cancer case has been operated upon at his clinic in the past two years. He says that the reason he stopped operating is because someone has to try out mesothorium in all kinds of cases for a long term of years to be able to render judgment in the future as to its real merits. He and *Kroenig* have decided to do so. His latest statistics are as follows: 145 cases treated of which 122 were uterine carcinomas—13 of these died. In 15 cases there is absolutely no objective or subjective symptoms noticeable at this time—10 of these were operable and 5 nonoperable cases or recurrences. He has never seen an operable case become worse after mesothorium was used. He has 350 mgm. of mesothorium divided into 50 mgm. capsules. He uses 100 mgm. doses, but this is due to the small amount he has."

"Dr. von *Seuffert,* his chief of clinic, thinks the best technique is to use 200 mgm. for 48 hours, repeated in 5 or 6 days for 24 hours or less, then discontinued for 3 weeks. He uses no lead stopper, but merely packs with gauze. He gets some slight tenesmus but not very much. This must be so, because I noticed that while in Bumm's clinic the patients feared the treatment; here they rather like it."

"*Kroenig* has 1700 mgm. of mesothorium and radium. The stand the Freiburg school taken on the operative interference with carcinoma, as told to me by *Gauss* is as follows: Where only a slight operation is required they operate and then ray; where a severe operation would be required, they never operate but only ray. Natives who can be kept under a long supervision are never operated upon, only rayed. Foreigners who can remain only a short time are often operated upon and then rayed. They generally combine the mesothorium with X-ray treatments. In deep-seated carcinomas they often dissect back the skin over the area affected, stitch back the flaps, and pour X-rays into the tissues *ad libitum.*"

"They think that systematic prophylactic treatments with hard filtered rays are of very decided value and should be carried out in every case. Of 23 cases treated in this way, after the lapse of one year 19 are still free—a decidedly better showing than they had in the past."

"*Czerny* and *Werner* at Heidelberg are doing very good work with their combination of enzytol, mesothorium and roentgentherapy. They have treated about 6,000 cases within the last 10 years. Werner's opinion at present is emphatically that all operable cases should be operated upon as soon as possible and then rayed."

"*Menge* has also stopped operating, but as he explains purely in an experimental way.

His technique is to insert 50 mgm. in 1 mm. gold filter, covered with about 2 mm. rubber and gauze into the cervix, and to place 50 mgm. on each side of the abdomen. This is left in place

for about 72 hours. Treatments are repeated at intervals of 3 weeks. He advises against the use of dermatol gauze as it produces secondary rays—plain sterilized gauze is the best."

In conclusion summarizing briefly the result of my observations during this short trip on the question of the present status of the non-operative treatments of malignant growths. "The question of proper dosage, filters, and other technique is a very complicated one which only years of work will solve." "The treatment with radioactive substances has shown sufficient results to justify the surgeon in discontinuing operations in cases of surface carcinoma and that of the mucous membranes easily reached, in patients who can be kept under long and continued observation, but in no other class of cases. In other cases, operative interference, followed by prophylactic raying, carried out systematically for years is still the best method of treatment." "There is practically no difference noticeable between the action of mesothorium and that of radium."

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A. Schuyler *Clark*. Radium Treatment of Cutaneous Epitheliomas by Single or Massive Doses. Journal Am. Med. Assn. Vol. 62, pp. 1453-8 (1914). Twenty-two case reports are given in which radium was used in the treatment of superficial growths of the face and neck. The author is of the opinion that it is better to make one long application of the radium rather than a series of exposures. His conclusions are as follows:—

"1. Radium is an efficient and satisfactory means with which to attack these lesions if used in sufficient quantity."

"2. The single or massive-dose method will probably prove to be the method of choice, as it has been in the hands of some of us in the Roentgen-ray treatment of these lesions."

"3. It is easier to estimate this single or massive dose because we are dealing with a stable remedy emitting a constant amount of rays, which is not the case with Roentgen rays, even with the pastiles now at our disposal."

"4. The cosmetic results are at least equal to those of any other form of treatment of these lesions."

"5. Its ease of application, comparative painlessness, even in the inflammatory stage, and harmless appearance recommend it to patients."

"6. The length of exposures can be practically determined and depends on the amount of radium and the character of its container, its distance from the lesion, the location of the lesion, the character of the lesion—whether superficial or deep—and the age, state of health and susceptibility of the patient to other rays, such as the sun's."

"7. Its two disadvantages are its high cost and the length of time of exposure in the single-dose method. This latter, however, is indirectly in proportion to the amount of radium employed."

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